REMARKS

Claim 1 has been amended to recite

> A vector or plasmid comprising an isolated DNA encoding vitamin B_6 phosphate phosphatase selected from the group consisting of:
>
> (a) the DNA sequence of SEQ ID NO:9;
>
> (b) a DNA sequence encoding a polypeptide having vitamin B_6 phosphate phosphatase activity, which hybridizes under stringent hybridization and stringent washing conditions to the DNA sequence defined in (a), wherein the stringent hybridization and stringent washing conditions comprise hybridizing in 5xSSC, 0.3% SDS, 2% blocking reagent, 0.1% N-lauroylsarcosine, 50% formamide overnight at 42°C and washing twice in 2xSSC, 0.1% SDS at room temperature for 5 minutes and then washing twice in 0.1xSSC, 0.1% SDS at 68°C for 15 minutes;
>
> (c) a DNA sequence encoding a polypeptide having vitamin B_6 phosphate phosphatase activity, wherein said polypeptide is at least 90% identical to the amino acid sequence of SEQ ID NO:10;
>
> (d) a DNA sequence encoding a polypeptide having vitamin B_6 phosphate phosphatase activity and is at least 90% identical to the DNA sequence of SEQ ID NO:9; and...

Support for these amendments may be found in the specification at, for example, page 3, lines 1-25; in Examples 1-2; and in original claim 1. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l) (8th ed. Rev. 7, July 2008, pp. 600-92, 600-93, and 600-84).

Claim 4 has been amended to recite

> Claim 4. (Previously Presented) A recombinant microorganism of the genus *Sinorhizobium* or *Escherichia*, capable of producing vitamin B_6 from vitamin B_6 phosphate, wherein said microorganism is transformed with a DNA encoding vitamin B_6 phosphate phosphatase selected from the group consisting of:
>
> (a) the DNA sequence of SEQ ID NO:9;

(b) a DNA sequence encoding a polypeptide having vitamin B_6 phosphate phosphatase activity, which hybridizes under stringent hybridization and stringent washing conditions to the DNA sequence defined in (a), wherein the stringent hybridization and stringent washing conditions comprise hybridizing in 5xSSC, 0.3% SDS, 2% blocking reagent, 0.1% N-lauroylsarcosine, 50% formamide overnight at 42°C and washing twice in 2xSSC, 0.1% SDS at room temperature for 5 minutes and then washing twice in 0.1xSSC, 0.1% SDS at 68°C for 15 minutes;

(c) a DNA sequence encoding a polypeptide having vitamin B_6 phosphate phosphatase activity, wherein said polypeptide is at least 90% identical to the amino acid sequence of SEQ ID NO:10;

(d) a DNA sequence encoding a polypeptide having vitamin B_6 phosphate phosphatase activity and is at least 90% identical to the DNA sequence of SEQ ID NO:9; and...

Support for these amendments may be found in the specification at, for example, page 3, lines 1-25; in Examples 1-2; and in original claim 4. (*Id.*)

Claim 14 has been amended to recite "...comprising the polynucleotide sequence of SEQ ID NO:9." Support for these amendments may be found in the specification at, for example, page 2, line 22 to page 4, line 9; SEQ ID NO: 9 and original claim 1. (*Id.*)

Claims 16-18 have been added. Support for these amendments may be found in the specification at, for example, page 1, lines 3-6 and lines 10-16; and page 5, lines 10 to page 6, line 14; and Examples 1 and 2 (pages 7-11).

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

§112, First Paragraph Rejection:

Enablement

Claims 1, 4, 7, 11 and 14 have been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. (Paper No. 20080730 at 2-6). The Examiner, however, stated that "[t]his rejection can be overcome by deleting 'fragments thereof' (part (b) line 3) and washing at '50[°]C' (part (b), line 7) and replacing the phrase 'comprising 2 polynucleotide sequence of SEQ ID NO: 9' with 'comprising the polynucleotide sequence of SEQ ID NO: 9' (claim 14) and, replacing 'a DNA sequence[']' (part a) of claims 1 and 4 with 'the DNA sequence'." (*Id.* at 6)

With a view towards furthering prosecution, claims 1 and 4 (from which claims 7, 11 depend), as well as claim 14, have been amended in accordance with the Examiner's suggestions. In view of the foregoing, it is believed that the rejection of claims 1, 4, 7, 11, and 14 has been rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

Written Description

A. Claims 1, 4, 7, 11 and 14

Claims 1, 4, 7, 11 and 14 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. (Paper No. 20080730 at 6-7). The Examiner, however, stated that "[t]his rejection can be overcome by replacing the phrase 'comprising a polynucleotide sequence of SEQ ID NO: 9' with 'comprising the polynucleotide sequence of SEQ ID NO: 9' (claim 14) and,

replacing 'a DNA sequence (part a) of claims 1 and 4 with "the DNA sequence'." (*Id.* at 7, emphasis original).

With a view towards furthering prosecution, claims 1 and 4 (from which claims 7, 11 depend), as well as claim 14, have been amended in accordance with the Examiner's suggestions. In view of the foregoing, it is believed that the rejection of claims 1, 4, 7, 11, and 14 has been rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

B. Claims 1, 4, 5-7 and 9-11

Claims 1 and 4, and dependent claims 5-7 and 9-11 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. (Paper No. 20080730 at 7-8). In making the rejection, the Examiner asserted that "[t]here is no indication in the specification of the recitation '95%' as recited in the claims, within the scope of the invention as conceived by Applicants at the time the application was filed." The Examiner required the cancellation of the alleged new matter.

With a view towards furthering prosecution, claims 1 and 4 have been amended to remove the recitation of "95%." In view of the foregoing, it is believed that the rejection of claims 1 and 4, and dependent claims 5-7 and 9-11 has been rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

Rejection Under 35 USC § 103:

Claims 1, 4, 7, 11, and 14 have been rejected under 35 USC § 103 as being unpatentable over Capela *et al.,* GenBank Accession No. AL591783 (nucleic

acid), August 2001, and GenBank Accession No. Q92SG4 (protein), December 2001) ("Capela") in view of "common knowledge." (Paper No. 20080730 at 8-10).

Capela discloses the sequence of a nucleic acid (GenBank Accession No. AL591783) and a protein (GenBank Accession No. Q92SG4).

In making the rejection, the Examiner asserted that Capela discloses "a putative oxidoreductase type protein encoded by the open reading frame (ORF), which is 99.5% identical to SEQ ID NO: 9 of the instant application, inherently a vitamin B6 phosphate phosphatase protein." (Paper No. 20080730 at 9).

The Examiner acknowledged, however, that Capela "do[es] not teach a vector comprising said sequence, [a] transformed host cell and a method of producing said protein in [a] transformed host cell and extraction of cell lysate." (*Id.* at 9-10).

To fill the acknowledged gap in Capela, the Examiner relied on "common knowledge" (*Id.* at 10). The Examiner asserted that "inserting an ORF of the nucleic acid of Capela et al. into a vector to produce the protein encoded by the open reading frame in order to determine its function is within the knowledge of the one of ordinary skilled in the art and which is widely used in the prior art for producing a new protein for functional studies." (*Id.*) The Examiner also asserted that "[o]ne of ordinary skill in the art would have been motivated for cloning the DNA of Capela et al. in a vector, transform an E. coli host cell, a process for producing the protein in said E. coli cell, extract the cell lysate, which is widely known in the art for producing a new protein for functional studies." (*Id.*) The Examiner also asserted that "[o]ne of ordinary skill in the art would have a reasonable expectation of success because cloning a gene, expression and a process for producing said protein is widely known and used in the art

for over-producing interested protein in bacterial system." (*Id.*) The Examiner concluded that " [i]t would have been obvious to one to [*sic*] ordinary skill in the art at the time of the invention was made to combine the teachings of Capela et al. with the common knowledge to clone the DNA of Capela et al. in a vector, transform an E. coli host cell, a process for producing said protein in E. coli cells, [and] preparing cell extract." (*Id.*)

The rejection is respectfully traversed.

Initially, we note that the Examiner failed to identify where in AL591783 it is disclosed that the translation product defined by the polynucleotide sequence encodes "a vitamin B_6 phosphate phosphatase." The Examiner merely asserted that Capela discloses that "a **putative** oxidoreductase type protein encoded by the open reading frame (ORF), which is 99.5% identical to SEQ ID NO: 9 of the instant application, inherently a vitamin B6 phosphate phosphatase protein." (Paper No. 20080730 at 10, emphasis added). As is shown from GenBank Accession No. AL591783 and GenBank Accession No. Q92SG4 (Uniprot), Capela does not indicate any function of the polypeptide sequence, and it is simply characterized as a "hypothetical protein." *See* GenBank Accession No. Q92SG4.

Recognizing these factual gaps, the Examiner sought refuge in the doctrine of inherency. Although it is well settled that, that which may be inherent is not necessarily known. Obviousness ***cannot*** be predicated on what is unknown. *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993) ("***That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.' Such a retrospective view of inherency is not a substitute for some teaching or***

suggestion supporting an obviousness rejection.") (citations omitted) (emphasis added). Thus, even if a claim is inherently anticipated, it may not be obvious. The Federal Circuit addressed this point by giving the following example:

> Consider...a claim directed toward a particular alloy of metal. The claimed metal alloy may have all the hallmarks of a nonobvious invention--there was a long felt but unresolved need for an alloy with the properties of the claimed alloy, others may have tried and failed to produce such an alloy, and, once disclosed, the claimed alloy may have received high praise and seen commercial success. Nevertheless, there may be a centuries-old alchemy textbook that, while not describing any metal alloys, describes a method that, if practiced precisely, actually produces the claimed alloy. While the prior art alchemy textbook inherently anticipates the claim under *§ 102*, **the claim may not be said to be obvious under *§ 103***. *Cohesive Technologies Inc. v. Waters Corp.*, 543 F.3d 1351, 1364, fn2 (Fed. Cir. 2008) (emphasis added).

Thus, the Examiner's rejection is legally deficient and should be withdrawn for this reason alone.

Furthermore, the rejection is also factually deficient. The Examiner failed to establish that Capela's hypothetical protein is "inherently a vitamin B6 phosphate phosphatase protein." (Paper No. 20080730 at 10). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted) "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to

reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

It is respectfully submitted that the Examiner failed to provide a basis for asserting that the hypothetical protein disclosed by Capela is necessarily a B_6 phosphate phosphatase. As acknowledged by the Examiner, Capela's DNA sequence differs in sequence from SEQ ID NO: 9 of the instant application. In fact, the protein encoded by Capela's DNA sequence encodes a hypothetical protein that differs from the polypeptide encoded by SEQ ID NO: 9 (or SEQ ID NO: 10) in at least 2 amino acid residues. (*See* sequence comparison dated 2/5/2007, mailed with Paper No. 20070206.) As it is well-known in the art and as acknowledged by the Examiner in a previous office action, "even small amino acid changes result in enzymatic activity changes." (Paper No. 20070206 at 10). For example, one of the articles cited by the Examiner, Witkowski *et al.* "Conversion of a beta-ketoacyl synthase to a malonyl decarboxylase by replacement of the active-site cysteine with glutamine" *Biochemistry*, 38(36):11643-50 (1999) ("Witkowski"), disclosed that change of a single amino acid converted a beta-ketoacyl synthase to a malonyl decarboxylase. (*E.g.,* Wuitkowski, abstract.) Furthermore, because Capela disclosed a "hypothetical protein," the Examiner also failed to establish whether this "hypothetical protein" has any activity at all, let alone B_6 phosphate phosphatase activity. It is well-known in the art that a single mutation can inactivate a protein. For example, the article cited by the Examiner in Paper No. 20070822, Guo *et al.*, "Protein tolerance to random amino acid change," *Proc Natl Acad Sci U S A.* 101(25):9205-10 (2004) ("Guo"), disclosed that for the

human DNA repair enzyme 3-methyladenine DNA glycosylase, the probability that a random amino acid replacement will lead to a protein's functional inactivation is 34% ± 6%. (*E.g.*, Guo, abstract). In view of the foregoing, there is no reasonable basis for the Examiner's assertion that "a putative oxidoreductase type protein encoded by the open reading frame (ORF), which is 99.5% identical to SEQ ID NO: 9 of the instant application" is "inherently a vitamin B6 phosphate phosphatase protein." (Paper No. 20080730 at 10). Therefore, the Examiner failed to establish that "the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *In re Robertson*, 169 F.3d 743, 745.

Again, the Examiner's conclusion is in direct conflict with the international preliminary examination report (IPER), which had AL591783 before it: "The present application relates to a vitamin B6 phosphate phosphatase ... ***which has not been disclosed before in the prior art***." (emphasis added) (Form PCT/Separate Sheet/409 (Sheet 1)); *see also* Form PCT/PEA/409 (concluding that all claims have novelty, inventive step, and industrial applicability).

Here, the overwhelming evidence is that Capela does not disclose a vitamin B_6 phosphate phosphatase, and the Examiner cannot fill this gap by hindsight reconstruction characterized as "common knowledge." For this further reason, the rejection has been rendered moot and must be withdrawn.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the objections and rejections, and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on February 23, 2009.

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Respectfully submitted,

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